UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/736,268	12/15/2000	Karen B. Chapman	P 0276580 23523-0169	8120

909 7590 08/13/2002

PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	9

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/736,268	Applicant(s) CHAPMAN, KAREN B.	
	Examin r David Lamberson	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05/30/02* .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *17-25 and 33-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,26-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-16 and 26-32 in Paper No. 5 is acknowledged.

Claims 17-25 and 33-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 5.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-11, and 26-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 recites the limitation "said cell" in line 1 of the claim. There is insufficient antecedent basis for this limitation in the claim. It is unclear if the applicant is referring to the donor cell or the recipient cell. Indication of which cell is indicated, the "donor" or the "recipient", will be remedial.

Claims 6-8 recite the limitation "said mammalian cell" in line 1 of each of the claims. There is insufficient antecedent basis for this limitation in the claim. Since it is unclear which

cell is a mammalian cell in Claim 5, it is also unclear which cell is a mammalian cell in claims 6-8. Defining the mammalian cell as indicated in Claim 5 will be remedial.

Claim 9 (and all dependent claims) is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. Specifically, applicant states that the "recipient cells are genetically modified prior, concurrent and/or subsequent to...", where it is unclear how the modification can be performed previously, concurrently and subsequently. Replacement of the "and/or" with "or" will be remedial.

The term "effective amount" in claim 26 (and all dependent claims) is a relative term which renders the claim indefinite. The term "effective amount" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The term "biologically pure" in claim 32 is a relative term which renders the claim indefinite. The term "biologically pure" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in

section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1, 2, 5, and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Willadsen (*Nature* 320: 63-65, 1987).

Claim1 is being interpreted (here, and in the following pages) to mean the physical contacting of the cytoplasm of a less differentiated cell (donor cell provides the cytoplasm) with the nucleus of a more differentiated cell (recipient cell provides the nucleus), where the more differentiated cell becomes reprogrammed or increases its life-span. As per applicant's definition, reprogramming equates to the conversion of a cell to a less differentiated cell type. In light of this definition, it is an inherent property that a cell becomes less differentiated solely upon the introduction of less differentiated material, as the cell would then contain less differentiated cellular matter and therefore be more primitive.

Willadsen describes a method of fusing an embryonic (blastomere, which applicant defines as substantially, but not totally, undifferentiated) cell from a ewe with an enucleated oocyte (e.g., the cytoplasm of the oocyte), wherein the embryonic cell is clearly more differentiated than the oocyte (see page 64, the abstract). Considering applicant's definition, this cell would then be less differentiated, and therefore reprogrammed. This is anticipatory of claims 1, 2, 5 and 6 because the cytoplasm is being donated to a more differentiated cell (claim 1) by an oocyte (claim 2) of a ewe (claims 5 and 6).

Claims 1, 2, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilmut, et al. (*Nature* 385:810-813, 1997).

Wilmut, et al., teaches the fusion of an adult mammary gland cell with an enucleated unfertilized egg, wherein the mammary gland cell is clearly more differentiated than the unfertilized egg, using sheep as the organism again (see page 810, the abstract and page 813, paragraphs 2 and 3 of the methods). Considering applicant's definition, this cell would then be less differentiated, and therefore reprogrammed. This is anticipatory of claims 1, 2, 5 and 6 because the cytoplasm is being donated to a more differentiated cell (claim 1) by an oocyte (claim 2) of a sheep (claims 5 and 6).

Claims 1, 2, 5-8, 14-16, 26, 28, 29, and 32 are rejected under 35 U.S.C. 102(e) as being anticipated by Robl, et al. (US Patent Publication 2001/0012513 A1).

Robl, et al., describes a method for the production of isogenic embryonic stem cells by transplantation of cell nuclei derived from animal or human cells into enucleated animal oocytes of a different species (see page 1, paragraph [002]), where the nuclei can be obtained from an adult differentiated human cell (see page 3, paragraph [0040] and [0042]). Considering applicant's definition, this cell would then be less differentiated, and therefore reprogrammed. This anticipates the aforementioned claims because the cytoplasm is being donated to a more differentiated cell (claim 1) by an oocyte (claim 2) using mammals, including humans (claims 5-8), where the transfer can occur across species, which inherently includes non-human primates and humans, for the production of embryonic stem cells (claims 14-16). Analogously, claims 26, 28, 29 and 32 are anticipated because culturing the embryonic stem cells (as a biologically pure culture) would be necessary in order to use the stem cells for any purpose.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 4, and 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willadsen in view of Thomson, et al. (*Science* 282:1145-1147, 1998), in further view of Greider, et al. (WO 97/35967).

The instant invention provides a method for reprogramming differentiated cells to a less differentiated state or altering the life-span of a cell by using the cytoplasm of a less differentiated "donor cell" and introducing it to a more differentiated cell "recipient cell". The invention recites limitations concerning what cells can be used in this method as well as the use of genetic modification of the "recipient cell" and the use of regulatable DNA constructs for the expression of telomerase. Lastly, the invention recites a limitation wherein embryonic stem cells are produced and cultured following the aforementioned limitations.

Willadsen teaches a method of fusing an embryonic (blastomere) cell from a ewe with an enucleated oocyte, as indicated above. Willadsen does not teach the introduction of telomerase or a corresponding DNA construct under the control of a regulatable promoter (claims 3 and 4), nor does it teach the introduction of genetic alterations for encoding a desired polypeptide (claims 9-12) or the increase in life-span of a mammalian cell (claim 13).

Thomson, et al., teaches that embryonic stem cells express high levels of telomerase, which corresponds with an increased life-span exceeding that of somatic cells (see page 1145, third column, first paragraph).

Greider, et al., teaches the use of a DNA construct with a regulatable promoter, where the introduction of the construct can result in genetic modification of the cell, therefore expression of telomerase activity at different levels (see Figure 4C and page 2, lines 18-25).

Willadsen is modified by Thomson, et al., and Greider, et al., by introducing the construct described by Greider, et al., to genetically alter (claims 9 and 10) the recipient cell (cell providing the nucleus), thereby providing a desired peptide (claim 11), that being telomerase (an enzyme, as in claim 12) in the form of a DNA construct containing a regulatable promoter element (claims 3 and 4), which in turn alters the life-span of the cell (claim 13) as indicated by Thomson, et al.

The ordinary skilled artisan would have been motivated to modify Willadsen in view of Thomson, et al., in further view of Greider, et al., because telomerase has been shown to be present at high levels of expression in embryonic stem cell increase the life-span of cells, as evidenced in Thomson, et al. Therefore, in the construction of an embryonic stem cell, it would be necessary to have high levels of telomerase in order to enhance the probability that the embryonic stem cells would be effective. It would have been obvious to make the modification because Greider, et al., provides an efficient construct to achieve a regulatable expression of telomerase activity in the cell.

Given the teachings of the stated prior art and the level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 3, 4, and 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilmut, et al. in view of Thomson (*Science* 282:1145-1147, 1998), in further view of Greider, et al. (WO 97/35967).

The invention is as described above.

Wilmut, et al., teaches the fusion of an adult mammary gland cell with an enucleated unfertilized egg, as indicated above. Wilmut, et al., does not teach the introduction of telomerase or a corresponding DNA construct under the control of a regulatable promoter (claims 3 and 4), nor does it teach the introduction of genetic alterations for encoding a desired polypeptide (claims 9-12) or the increase in life-span of a mammalian cell (claim 13).

Thomson, et al., teaches that embryonic stem cells express high levels of telomerase, which corresponds with an increased life-span exceeding that of somatic cells (see page 1145, third column, first paragraph).

Greider, et al., teaches the use of a DNA construct with a regulatable promoter, where the introduction of the construct can result in genetic modification of the cell, therefore expression of telomerase activity at different levels (see Figure 4C and page 2, lines 18-25).

Wilmut, et al., is modified by Thomson, et al., and Greider, et al., by introducing the construct described by Greider, et al., to genetically alter (claims 9 and 10) the recipient cell (cell providing the nucleus), thereby providing a desired peptide (claim 11), that being telomerase (an enzyme, as in claim 12) in the form of a DNA construct containing a regulatable promoter element (claims 3 and 4), which in turn alters the life-span of the cell (claim 13) as indicated by Thomson, et al.

The ordinary skilled artisan would have been motivated to modify Wilmut, et al., in view of Thomson, et al., in further view of Greider, et al., because telomerase has been shown to be present at high levels of expression in embryonic stem cell increase the life-span of cells, as evidenced in Thomson, et al. Therefore, in the construction of an embryonic stem cell, it would be necessary to have high levels of telomerase in order to enhance the probability that the embryonic stem cells would be effective. It would have been obvious to make the modification because Greider, et al., provides an efficient construct to achieve a regulatable expression of telomerase activity in the cell.

Given the teachings of the stated prior art and the level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 3, 4, 9-13, 27, 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robl, et al., in view of Thomson (*Science* 282:1145-1147, 1998), in further view of Greider, et al. (WO 97/35967).

The invention is as described above.

Robl, et al., describes a method for the production of isogenic embryonic stem cells by transplantation of cell nuclei derived from animal or human cells into enucleated animal oocytes of a different species, where the nuclei can be obtained from an adult differentiated human cell, as indicated above. Robl, et al., does not teach the introduction of telomerase or a corresponding DNA construct under the control of a regulatable promoter (claims 3 and 4), nor does it teach the introduction of genetic alterations for encoding a desired polypeptide (claims 9-12) or the

increase in life-span of a mammalian cell (claim 13), or the analogous claims as it concerns the culturing of embryonic stem cells (claims 27, 20 and 31).

Thomson, et al., teaches that embryonic stem cells express high levels of telomerase, which corresponds with an increased life-span exceeding that of somatic cells (see page 1145, third column, first paragraph).

Greider, et al., teaches the use of a DNA construct with a regulatable promoter, where the introduction of the construct can result in genetic modification of the cell, therefore expression of telomerase activity at different levels (see Figure 4C and page 2, lines 18-25).

Robl, et al., is modified by Thomson, et al., and Greider, et al., by introducing the construct described by Greider, et al., to genetically alter (claims 9 and 10) the recipient cell (cell providing the nucleus), thereby providing a desired peptide (claim 11), that being telomerase (an enzyme, as in claim 12) in the form of a DNA construct containing a regulatable promoter element (claims 3 and 4), which in turn alters the life-span of the cell (claim 13) as indicated by Thomson, et al. Similarly, these modifications would be pertinent to the analogous claims concerning the embryonic stem cells (claims 27, 20 and 31).

The ordinary skilled artisan would have been motivated to modify Robl, et al., in view of Thomson, et al., in further view of Greider, et al., because telomerase has been shown to be present at high levels of expression in embryonic stem cell increase the life-span of cells, as evidenced in Thomson, et al. Therefore, in the construction of an embryonic stem cell, it would be necessary to have high levels of telomerase in order to enhance the probability that the embryonic stem cells would be effective. It would have been obvious to make the modification

because Greider, et al., provides an efficient construct to achieve a regulatable expression of telomerase activity in the cell.

Given the teachings of the stated prior art and the level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A Lambertson
August 12, 2002

DAVID GUZO
PRIMARY EXAMINER